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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/771,161	LEVINE ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1,2,4-11,15-32,34 and 35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3 and 12-14* is/are rejected.

7)☒ Claim(s) *3 and 12-14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *0401*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of Invention II, Claims 12-14, in part, 3, and 33, as well as SEQ ID NO: 2 and 93, in their response of October 20, 2003 is acknowledged. The traversal is on the ground(s) that –the Examiner provides no basis for requiring election of a single sequence of one of SEQ ID NO: 1-91 or encoding 92-182.– This argument is not found to be persuasive. SEQ ID NO: 1-91 and 92-182, each represent a distinct sequence. The reason for requiring election of a single sequence is that, a search of one sequence would not encompass a search for any other sequence and searching all sequences would represent a burden on the Office. Omission of Group II from the last three lines of page 2 is an obvious typographical error. The requirement is still deemed proper and is therefore made FINAL.

Claims 1-35 are pending. Claims 1, 2, 4-11, 15-32, 34, and 35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Inventions, there being no allowable generic or linking claim. Claims 12-14, in part, 3, and 33 are hereby considered on their Merits.

Specification-Objections

The specification is objected to for failing to claim priority, as the first paragraph, to applications listed as priority documents in the Oath/Declaration.

Claims-Objections

Claims 3, 12-14, and 33 are objected to for being dependent on non-elected claims.

Claims 3, 12-14, and 33 are objected to for reciting non-elected subject matter: SEQ ID NO: 1, 3-92, and 94-182.

In Claim 3, –coded– on lines 2 and 7 should be amended to –encoded–.

In Claim 3, for –sequences differs– on line 6, the subject and verb do not agree.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 12-14, and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is indefinite and confusing. Claim 3 is indefinite for failing to identify the parent sequence from which the recited sequences are derived. Claim 3(ii) is especially confusing in the recitation of "... where the amino acid sequences differs from the original amino acid sequence, coded by the original nucleic acid sequence from which the variant has been varied by alternative splicing...". Claim 3 should be rewritten to concisely recite the intended invention. Claims 12-14 and 33, as dependent on Claim 3, are rejected for the same reasons.

In Claims 14 and 33, the phrases –activity of kinase enzyme– and –kinase activity–, respectively, are indefinite. It is not clear whether the claims refer to, for example, the enzymatic activity of a kinase, down-stream signaling of a kinase, a final cellular response triggered by a kinase, or a disease due to over activity of a kinase. Clarification is required. For purposes of examination, it is assumed that said phrases refer to kinase enzymatic activity or any biochemical or cellular process that is stimulated by a kinase.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In this regard, the application disclosure and claims are compared per the factors indicating in the decision re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claims 3, 12-14, and 33 are rejected under 35 U.S.C. 112, first paragraph. The specification is enabling for using the polypeptide of SEQ ID NO: 93. However, the specification does not reasonably provide enablement for using any polypeptide encoded by SEQ ID NO: 2 or variants or fragments thereof or the polypeptide of SEQ ID NO: 93 or any variants or fragments thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 3 and 12 are so broad as to encompass the polypeptide encoded by SEQ ID NO: 2, and any variants or fragments thereof, and the polypeptide of SEQ ID NO: 93, and variants or fragments thereof. Claim 13 is so broad as to encompass pharmaceutical compositions, comprising any polypeptide encoded by SEQ ID NO: 2, or variants or fragments thereof, or the

polypeptide of SEQ ID NO: 93, or any variants or fragments thereof, which can be used for treatment of any disease that can be ameliorated or cured by raising the level of said polypeptide. Claim 14 is so broad as to encompass pharmaceutical compositions, comprising any polypeptide encoded by SEQ ID NO: 2, or variants or fragments thereof, or the polypeptide of SEQ ID NO: 93, or any variants or fragments thereof, which can be used for treatment of any disease that can be ameliorated or cured by inhibiting the activity of any kinase enzyme. Claim 33 is so broad as to encompass the polypeptide encoded by SEQ ID NO: 2, and any variants or fragments thereof, and the polypeptide of SEQ ID NO: 93, and variants or fragments thereof, wherein the polypeptide is an inhibitor of any kinase. The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides, diseases to be treated, and kinases to be inhibited, as broadly encompassed by the claims.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of SEQ ID NO 93 and the nucleotide sequence of SEQ ID NO 2. While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable

expectation of success in obtaining the desired activity/utility, including inhibiting the activity of any kinase, are limited in any protein and the results of such modifications are unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

Since the underlying biochemical and cellular problems determine the pathology of any disease, predictability of which diseases can be treated with the recited polypeptides requires a knowledge of and guidance with regard to which biochemical and cellular problems are affected by said polypeptides and a detailed knowledge of the ways in which said polypeptides relate to the biochemical and cellular mechanisms underlying any disease. In the instant application, the disclosure fails to disclose which diseases can be treated with the recited polypeptides. Techniques for determining the biochemical and cellular mechanisms underlying any disease, for synthesizing polypeptides derived from SEQ ID NO: 93, and for testing said compounds in *in vitro*, cellular, and animal models of many diseases are known. However, it is not routine in the art to determine whether the mechanisms underlying any disease are relevant to treatment with the recited polypeptides. It is also not routine to synthesize and test any variant polypeptide derived from SEQ ID NO: 93 as an inhibitor of any kinase or to test all said compounds in *in vitro*, cellular, and animal models of any disease. The number of diseases to be treated or prevented with a reasonable expectation of success using the recited polypeptides is limited and the results of treating any disease with said polypeptides is unpredictable.

The specification does not support the broad scope of Claims 3 and 12 which encompasses any polypeptide encoded by SEQ ID NO: 2 and any variants or fragments thereof as well as the polypeptide of SEQ ID NO: 93 and any variants or fragments thereof. The

specification does not support the broad scope of Claim 13 which encompasses pharmaceutical compositions, comprising any polypeptide encoded by SEQ ID NO: 2, and variants or fragments thereof, as well as the polypeptide of SEQ ID NO: 93, and variants or fragments thereof, which can be used for treatment of any disease that can be ameliorated or cured by raising the level of said polypeptide. The specification does not support the broad scope of Claim 14 which encompasses pharmaceutical compositions, comprising any polypeptide encoded by SEQ ID NO: 2, and variants or fragments thereof, as well as the polypeptide of SEQ ID NO: 93, and variants or fragments thereof, which can be used for treatment of any disease that can be ameliorated or cured by inhibiting the activity of any kinase enzyme. The specification does not support the broad scope of Claim 33 which encompasses any polypeptide encoded by SEQ ID NO: 2, and variants or fragments thereof, as well as the polypeptide of SEQ ID NO: 93, and variants or fragments thereof, wherein the polypeptide inhibits any kinase. The specification does not support the broad scope of Claims 3, 12-14, and 33 because the specification does not establish: (A) regions of the protein structure set forth by SEQ ID NO: 93 which may be modified without effecting the desired activity; (B) the general tolerance of the activity of the recited polypeptides to modification and extent of such tolerance; (C) which diseases can be treated with the recited polypeptides; (D) which kinases can be inhibited with the recited polypeptides; (E) a rational and predictable scheme for modifying any residues within the polypeptide of SEQ ID NO: 93 an expectation of obtaining the desired biological function; (F) a rational and predictable scheme for choosing which diseases to be treated with the recited polypeptides; (G) a rational and predictable scheme for choosing which kinases can be inhibited with the recited polypeptides; and (H) the specification provides insufficient guidance as to

which of the essentially infinite possible choices of polypeptides to be used, diseases to be treated, and kinases to be inhibited is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of polypeptides with an enormous number of amino acid modifications of SEQ ID NO: 93 or said polypeptides that can be used in the treatment of any disease or in the inhibition of any kinase. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 3, 12-14, and 33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 3 and 12 are directed to a genus of polypeptides including the polypeptide encoded by SEQ ID NO: 2, and variants or fragments thereof, as well as the polypeptide of SEQ ID NO: 93, and any variants or fragments thereof.

The specification does not contain any disclosure of the function of all said polypeptides. The genus of polypeptides that comprise these above protein molecules is a large variable genus with the potentiality of having many different functions. Therefore, many functionally unrelated polypeptides are encompassed within the scope of these claims, including partial peptide

sequences. The specification discloses the function of only a single species of the claimed genus, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 13, 14, and 33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 13 is directed to a genus of protein molecules that can be used for the treatment of any disease (Claim 13), while Claim 14 is directed to a genus of protein molecules that can be used to inhibit any kinase. The specification does not disclose any diseases to be treated with the recited polypeptides and discloses only one kinase to be inhibited with said polypeptides. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of either being useful in the treatment of any disease or the inhibition of any kinase. Given this lack of description of representative species encompassed by the genera of the Claims 13 and 14, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3, 12-14, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Wallach et al, 1998, Bertin et al, 1999, or Inohara et al, 1998. Wallach et al teach a polypeptide that comprises residues 6-232 of SEQ ID NO: 93. The polypeptide of Wallach et al is encoded by a polynucleotide having 783 contiguous nucleotides that are identical to SEQ ID NO: 2 but are not identical to AF027706. Wallach et al further teach pharmacological compositions comprising their peptide, and fragments thereof (pg 14, line 26-pg 15, line 3), as well as the use of said fragments to neutralize the kinase activity of B1 kinase (pg 31, line 5-6). Bertin et al teach a polypeptide that comprises residues 6-232 of SEQ ID NO: 93. The polypeptide of Bertin et al is encoded by a polynucleotide having 99.9% identity with residues 333-1065 of SEQ ID NO: 2, wherein said residues are not identical to AF027706. Bertin et al further teach pharmacological compositions comprising their polypeptide, and fragments thereof (pg 72, parg 1), as well as the use of said fragments to neutralize the kinase activity of CARD, a serine/threonine kinase (pg 50, parg 2). Inohara et al teach a polypeptide homolog of SEQ ID NO: 93 wherein the amino acids that differ from the original sequence have been varied (Fig 1).

Inohara et al also teach a polypeptide homolog of SEQ ID NO: 93 that is encoded by a nucleic acid sequence having at least 90% identity with SEQ ID NO: 93, wherein said polypeptide is a kinase inhibitor (Fig 3C). Pharmacological compositions comprising the polypeptides of Inohara et al are also taught (Fig 3D). Therefore, Claims 3, 12-14, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Wallach et al, 1998, Bertin et al, 1999, or Inohara et al, 1998.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sheridan Lee Swope, Ph.D.

Rebecca Prunier
1600